

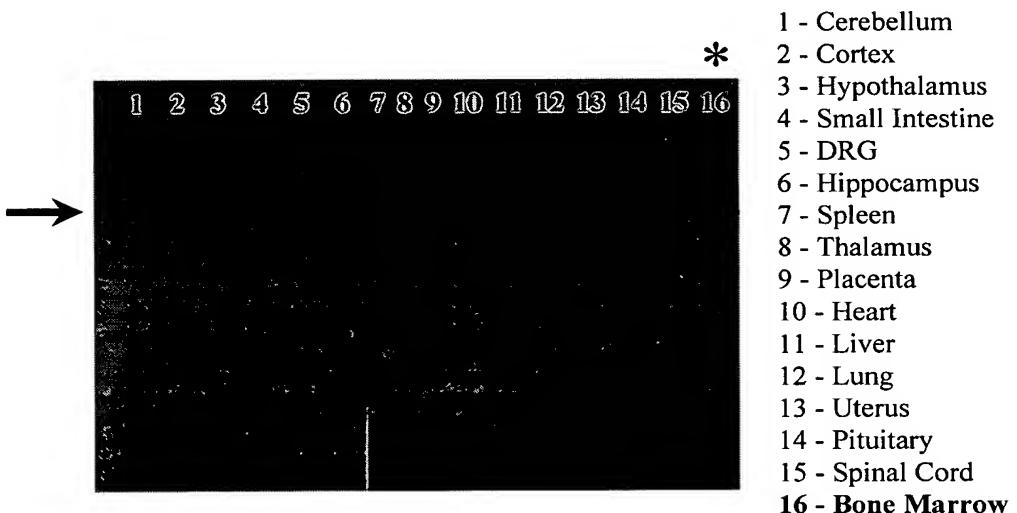
**Figure 1: Nucleic Acid coding sequence human histamine H4**

ATGCCAGATACTAATAGCACAAATCAATTACTACTAAGCACTCGTGTACTTAGCATT  
TTTATGTCCTTAGTAGCTTTGCTATAATGCTAGGAAATGCTTGGTCATTTAGCTTTG  
TGGTGGACAAAAACCTAGACATCGAAGTAGTTATTTTTCTTAACCTGGCCATCTCG  
ACTCTTGTGGGTGTGATCTCATTCTTGACATCCCTCACACGCTGTCGAATGGG  
ATTTGAAAGGAAATCTGTGTTAGGCTCACTACTGACTATCTGTTATGTACAGCAT  
CTGTATATAACATTGCTCATCAGCTATGATCGATACCTGTCAGTCTCAAATGCTGTG  
CTTATAGAACTCAACATACTGGGTCTTGAAGATTGTTACTCTGATGGTGGCCGTTGG  
GTGCTGGCCTCTTAGTGAATGGGCAATGATTCTAGTTCAAGAGTCTTGAAGGATGA  
AGGTAGTGAATGTGAACCTGGATTTCGAATGGTACATCCTGCCATCACATCATT  
CTTGGAAATTGATCCCAGTCATCTAGTCGCTTATTCAACATGAATATTATTGGAG  
CCTGTGGAAGCGTGATCATCTCAGTAGGTGCCAAGGCCATCTGGACTGACTGCTGTCT  
CTTCCAACATCTGGACACTCATTCAAGAGGTAGACTATCTCAAGGAGATCTCTTCTG  
CATCGACAGAAGTTCCTGCATCCTTCATTCAAGAGAGACAGAGGAGAAAGAGTAGTCTC  
ATGTTTCCTCAAGAACCAAGATGAATAGCAATACAATTGCTCCAAATGGGTTCTT  
CTCCCAATCAGATTCTGATGCTCTCACCAAGGGAACATGTTGAAGTCTAGAGCCA  
GGAGATTAGCAAGTCACTGCCATTCTTAGGGTTTGTCTGCTGGCTCCAT  
ATTCTCTGTTACAATTGTCCTTCAATTCTCAGCAACAGGTCTAAATCAGTTG  
GTATAGAATTGCAATTGGCTTCAGTGGTTCAATTCTTGTCAATCCTCTTGTATCCA  
TTGTGTACAAGCGCTTCAAAAGGTTCTGAAAATATTGTATAAAAAGCAACC  
TCTACCATCACAACACAGTCGGTCAGTATCTCTTAA

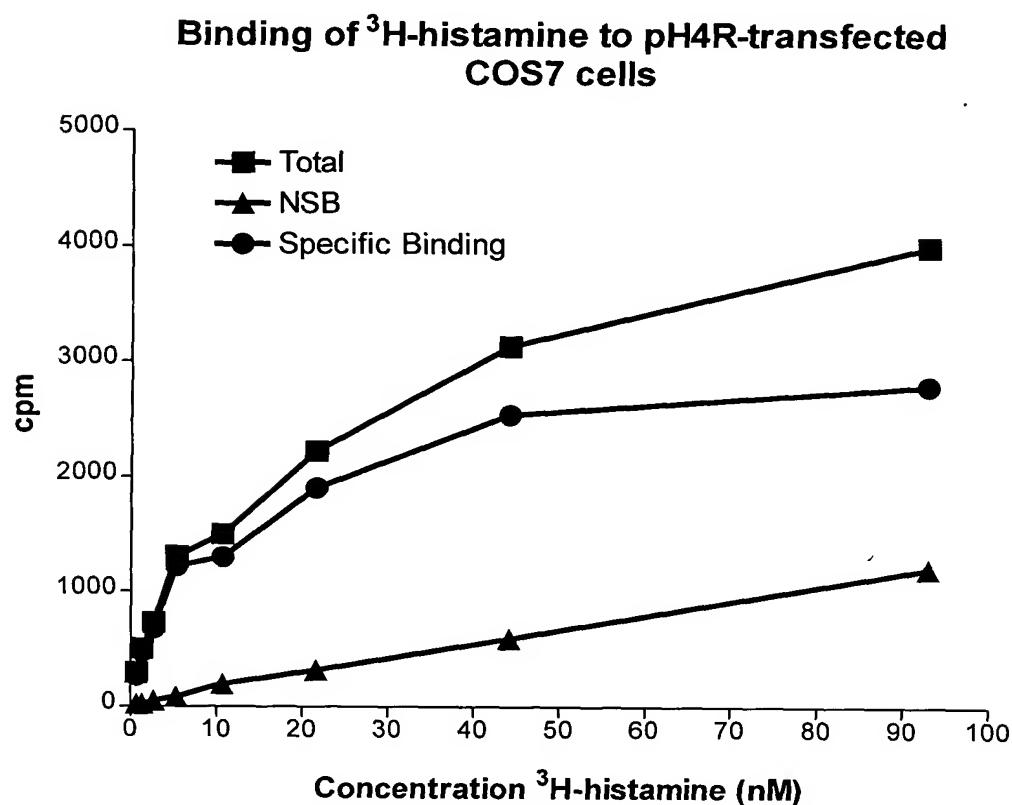
**Figure 2: Amino acid sequence human histamine H4 receptor**

Met Pro Asp Thr Asn Ser Thr Ile Asn Leu Ser Leu Ser Thr Arg Val Thr Leu  
Ala Phe Phe Met Ser Leu Val Ala Phe Ala Ile Met Leu Gly Asn Ala Leu Val  
Ile Leu Ala Phe Val Val Asp Lys Asn Leu Arg His Arg Ser Ser Tyr Phe Phe  
Leu Asn Leu Ala Ile Ser Asp Phe Phe Val Gly Val Ile Ser Ile Pro Leu Tyr  
Ile Pro His Thr Leu Phe Glu Trp Asp Phe Gly Lys Glu Ile Cys Val Phe Trp  
Leu Thr Thr Asp Tyr Leu Leu Cys Thr Ala Ser Val Tyr Asn Ile Val Leu Ile  
Ser Tyr Asp Arg Tyr Leu Ser Val Ser Asn Ala Val Ser Tyr Arg Thr Gln His  
Thr Gly Val Leu Lys Ile Val Thr Leu Met Val Ala Val Trp Val Leu Ala Phe  
Leu Val Asn Gly Pro Met Ile Leu Val Ser Glu Ser Trp Lys Asp Glu Gly Ser  
Glu Cys Glu Pro Gly Phe Phe Ser Glu Trp Tyr Ile Leu Ala Ile Thr Ser Phe  
Leu Glu Phe Val Ile Pro Val Ile Leu Val Ala Tyr Phe Asn Met Asn Ile Tyr  
Trp Ser Leu Trp Lys Arg Asp His Leu Ser Arg Cys Gln Ser His Pro Gly Leu  
Thr Ala Val Ser Ser Asn Ile Cys Gly His Ser Phe Arg Gly Arg Leu Ser Ser  
Arg Arg Ser Leu Ser Ala Ser Thr Glu Val Pro Ala Ser Phe His Ser Glu Arg  
Gln Arg Arg Lys Ser Ser Leu Met Phe Ser Ser Arg Thr Lys Met Asn Ser Asn  
Thr Ile Ala Ser Lys Met Gly Ser Phe Ser Gln Ser Asp Ser Val Ala Leu His  
Gln Arg Glu His Val Glu Leu Leu Arg Ala Arg Arg Leu Ala Lys Ser Leu Ala  
Ile Leu Leu Gly Val Phe Ala Val Cys Trp Ala Pro Tyr Ser Leu Phe Thr Ile  
Val Leu Ser Phe Tyr Ser Ser Ala Thr Gly Pro Lys Ser Val Trp Tyr Arg Ile  
Ala Phe Trp Leu Gln Trp Phe Asn Ser Phe Val Asn Pro Leu Leu Tyr Pro Leu  
Cys His Lys Arg Phe Gln Lys Ala Phe Leu Lys Ile Phe Cys Ile Lys Lys Gln  
Pro Leu Pro Ser Gln His Ser Arg Ser Val Ser Ser

**Figure 3: Tissue Distribution of human histamine H4 receptor**



**Figure 4: Binding of  $^{3}\text{H}$ -histamine to pH4R expressing COS7 cells.**



**FIGURE 5A**

**Mouse H4 DNA coding region (SEQ.ID.NO.:5)**

```
ATGTCGGAGTCTAACAGTACTGGCATCTGCCACCAGCTGCTCAGGTCCCTGGCATTAAATGT
CTTCATTGCCTTGCTATAATGGTAGGCAATGCTGTGGCATCTAGCCTTGTGGACAGAAA
CCTTAGACATCGAAGTAATTATTTCTTAATTGGCTATTCTGACTTCCTCGTGGGTTGATT
TCCATTCCCTGTACATCCCTACGTGTGTTAACTGGAATTGGAAAGTGAATCTGCATGTTT
GGCTCATTACTGACTATCTTGTGCACCGCATCTGCTACAAATATTGCTCTCATTAGCTACGATCG
ATACCAGTCAGTTCAAATGCTGTCTTATAGGGCTAACACACTGGCATCATGAAGATTGTTGCT
CAAATGGTGGCTGTTGGATACTGGCTTCTGGTAAATGGCCCGATGATTCTGGCTTCAGATTCTT
GGAAGAACAGCACGAACACAAAGGACTGTGAGCCTGGCTTGTACAGAGTGGTACATCCTCACCAT
TACAATGCTCTTGGAAATTCCCTGCTTCGTACATCTGTGGCTTATTCAATGTACAGATTACTGG
AGCCTGTGGAAGCGTAGGGCTCTCAGTAGGTGCCCTAGCCATGCTGGATTCTCCACTACCTCTCCA
GTGCTTCAGGACACTTACACAGAGCTGGGTGGCTGAGGACAAGTAATCCTGGATTGAAGGAATC
AGCTGCATCTCGTCACTCAGAAAGTCCTCGAAGAAAGAGCAGCAGCATCCTGGTGTCTTAAGGACTCAC
ATGAACAGCAGTATCAGTGCCTTCAAAGTGGGTTCTGGCGATCGGAAAGTGCAGCGCTCGCC
AAAGGGAGTACGCAGAGCTCTCAGAGGAGGAAGCTAGCCAGGTCACTGCCATCCTCTGAGCGC
TTTGCCATTGCTGGCTCCATACTGTCGTTACAATTGCTCTTCAACTTACCCAGAACGGAA
CGCCCCAAATCGGTGGTACAGCATTGCCCTCTGGCTGCAATGGTTCAATTGTTAATCCCT
TTCTGTACCCCTTGTGTCACAGGCCTTCCAGAAGGCTTCTGGAAGATACTTGTGACAAAGCA
ACCAGCGCTGTCACAGAACCAAGTCAGTATCTTCTGA
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**FIGURE 5B**

**Rat H4 DNA coding region (SEQ.ID.NO.:6)**

```
ATGTCGGAGTCTAACGGCACTGACGTCTGCCACTGACTGCTCAAGTCCCCTGGCATTAAATGT
CCCTGCTGCTTTGCTATAACGATAGGCAATGCTGGTCATTTAGCCTTGTAGCAGACAGAAA
CCTTAGACATCGAAGTAATTATTTCTTAATTGGCTATTCTGACTCTCGTGGGTGTCATC
TCCATT CCTCTGTACATCCCTCACACGCTTTA ACTGGAATTGGAAAGTGGAACTGCATGTTT
GGCTCATTACTGACTATCTTGTGCACAGCATCCGTCTACAGTATTGTCCTCATTAGCTACGATCG
ATACCAGTCAGTTCAAACGCTGTGCGTTAGAGCACAGCACACTGGCATCCTGAAAATTGTTGCT
CAAATGGTGGCTGTTGGATACTGGCTTCTGGTCAATGGCCAATGATTCTGGCTCGGATTCTT
GGAAGAACAGCACCAACACAGAGGAGTGCAGCAGCCTGGCTTGTACTGAGTGGTACATCCTGCCAT
TACAGCATTCTGGAATT CCTGCTCCCTGTCTCCTGGTGGCTATTCACTGAGTGGTACAGATTACTGG
AGCCTGTGGAAGCGTGGGAGTCTCAGTAGGTGCCCTAGCCACGCTGGATTCATCGCTACCTCTCCA
GGGGCACTGGACACTCACGCAGAACTGGGTTGGCTGTAGGACAAGTCTCCTGGATTAAAGGAACC
AGCCGCATCCCTCATTCAAGAAAGTCCACGAGGAAAGAGCAGTCTCCTGGTGTCTTAAGGACTCAC
ATGAGCGGTAGTATCATGCCCTCAAAGTGGGTTCTGCGATCAGAAAGCCCAGTGCTTCACC
AGAGAGAGCACGTGGAGCTCTCAGAGGCAGGAAGCTAGCCAGGTGCTAGCTGTCTCCTGAGTGC
TTTGCCATTGCTGGCTCCGTATTGCTGTTCAACAATTGTTCTTCAACTATCGCAGAGGGAG
CGCCCCAAATCGATTGGTACAGCATGCCCTGGCTACAGTGGTCAATTCACTTATTAAATCCCT
TTCTATACCCTTGTGCCACAGACGTTCCAGAAGGCTTCTGGAAGATACTCTGTGTGACAAAGCA
ACCAGCACCTTCACAGACCCAGTCAGTATCTTCTTGA
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### FIGURE 5C

Guinea Pig H4 DNA coding sequence (SEQ.ID.NO.:7)

```
ATGTTGGCAAATAACAGTACAATGCCCTAACATCAATTAAAATTCTTGACATTTTA
ATGTCTTACTAGCTATTGCTATAATGTTAGGCAATGCGTGGTCATTTAGCTTTATTG
TGGACAGAAATCTTAGACATCGAAGTAATTACTTTCTTAACCTGGCCATTGCAGACT
TCTTGTGGGTGCAATTGCAATTCCCTCTGTACATACCTCCTCGCTGACTTACTGGACTT
CTGGAAAGCAAGCTTGTATTGGCTATTACTGACTATCTTTATGtACAGCATCTGT
GTATAATATTGTCCATCAGCTACGATCGCTACAGTCAGTCTCAAATGCCGTGTGGTA
TAGAGCTCAGCACTCTGGCACCTGGAAAATTGCTACTCAGATGGTGGCTTTGGATAT
TCTCCTTCATGACAAATGGCCGATGATTCTGATTCAGACTCTGGCAGAATAGCACT
ACAGAATGTGAACCTGGATTAAAAGTGGTACTTGCTCTCCCTACATCATTATTG
GAATTCCCTGATCCCCATCTGTTAGTTGCTTATTCAGCGCCCATTTACTGGAGCCTG
TGGAAAGCGAGAGAAAAGTGCAGCTGGCTCAGCCACCCCTGTACTCCCTCTGACTCTTC
CAGCAGTGACCACGGACACTCCTGCAGACAGGACCCGATTCAAGGGCGACTCTGCCA
GCACGGAAAGAAACAACGTGCCTCTTGTTCAAGACAAGTCACGGAGAAAGAGCAGTC
TCTTGTCCATAAGAGCCTACAAGAACAGCAATGTGATCGCTTCAAAATGGCTTC
CTCTCCCACTCAGATTCCCTGGCTTCAAGACAAGGAACATATCGAACCTTCAGAGC
CAGGAAATTAGCCAAGTCACTGGCCATACTCTAGCAGCTTGCCTTGGCTCC
ATATTCACTGACTACAGTTACTCATTTCCTGAAAGGAACCTGACTAAATCAAC
CTGGTACCAACTGCCTTGGCTCCAGTGGTCAATTCTTGTAAATCCCTTGTAT
CCATTGTGTCACAAACGTTTCAGAAGGCTTCAGAAAGGAAACTTCCCTGTGAGAAGGCA
ATCCACGCCACCACACAACCGCTCAATATCCACTTGA
```

**FIGURE 6A**

Mouse histamine H4 receptor protein sequence (SEQ.IDN.NO.:8)

MSESNSTGILPPAAQVPLAFLMSSFAFAIMVGNAVVILAFVVDRNLRHRSNYFFLNL AISDFL  
VGLISIPLYIPHVLFNWNFGSGICMFWLITDYLCTASVYNIVLISYDRYQSVSNAVSYRAQH  
TGIMKIVAQMVAVWILAFLVNGPMILASDSWKNSTNTKDCEPGFVTEWYILTITMLLEFLLP  
VISVAYFNQIYWSLWKRRALSRCPSHAGFSTTSSASGHLHRAGVACRTSNPGLKESAASR  
HSESPRRKSSILVSLRTHMNSSITAFKVGSFWRSESAALRQREYAELLRGRKLARSLAILLSA  
FAICWAPYCLFTIVLSTYPRTERPKSVWYSIAFWLQWFNSFVNPFLYPLCHRRFQKAFWKIL  
CVTKQPALSQNQS VSS

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**FIGURE 6B**

Rat histamine H4 receptor protein sequence (SEQ.ID.NO.:9)

MSESNGTDVLPLTAQVPLAFLMSLLAFAITIGNAVVILAFVADRNLRHRSNYFFLNLAISDFF  
VGVISIPLYIPHTLFNWNFGSGICMFWLITDYLCTASVYSIVLISYDRYQSVSNAVRYRAQH  
TGILKIVAQMVAVWILAFLVNGPMILASDSWKNSTNTEECEPGFVTEWYILAITAFLEFLLPV  
SLVVYFSVQIYWSLWKRGSLSRCPSHAGFIATSSRG TGHSRRTGLACRTSLPGLKEPAASLH  
SESPRGKSSLVSLRTHMSGIIAFKVGSFCRSESPV LHQREHVELLRGRKLARSLAVLLSAF  
AICWAPYCLFTIVLSTYRRGERPKSIWYSIAFWLQWFNSLINPFLYPLCHRRFQKAFWKILCV  
TKQPAPSQTQSVSS

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**FIGURE 6C**

Guinea Pig histamine H4 receptor protein sequence (389 amino acids)  
(SEQ.ID.NO.:10)

MLANNSTIALTSIKISLTFLMSLLAIAIMLGNNVVVILAFIVDRNLRHRSNYFFLNLAIAFFVG  
AIAIPLYIPSSLTYWTSGKQACVFWLITDYLCTASVYNIVLISYDRYQSVSNAVWYRAQHS  
GTWKIATQMVAVWIFSFMNTNGPMILISDSWQNSTTECEPGFLKKWYFALPTSLLEFLIPILLV  
AYFSAHIYWSLWKREKLSRCLSHPVLPSSSDHGHSCRQDPDSRATLPARKETTASLGSD  
KSRRKSSLFSIRAYKNSNVIASKMGFLSHDSLALQQREHIELFRARKLAKSLAILAAFAIC  
WAPYSLTTVIYSFFPERNLTKSTWYHTAFWLQWFNSFVNPFYPLCHKRFQKAFLKILPVRR  
QSTPPHNRSIST

**Figure 7A**  
**Nucleotide Sequence Comparison of Human (SEQ ID NO:1), Guinea Pig (SEQ ID NO:7), Mouse (SEQ ID NO:5), and Rat H4 (SEQ ID NO:6)**

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**Figure 7B**

Human: CCATATTCTGTTCACAAATTGCTCTTCAATTTCAGCAACAGGTCTTAATCAGTTGGCTTCAGTGGTCATTGCAATTCCCTTGCTCAATCCTCTTGT 1071  
 Guinea Pig: CCATATTCTACTGACTAACAGTTATCTAATTCATTTCCTGAAAGGAATCTGACTTAATCAGCTTGGTACCATACTGCTTGGCTTCAGTGGTCATTGCAATTCCCTTGT 1071  
 Mouse: CCATACTCTGTTCACAAATTGCTCTTCAACTAACCCAGAACGAAAGGCCAACATGGTGGTACAGATGCGCTTCTGGTCAATGGTCATTGCAATTCCCTTGT 1077  
 Rat: CGTATGGCTGTTCAAAATTGCTTCAACTTAATGCAAGGGAGCGCCCAATCGATTTGCTACAGTGGTCATTCAACTTAATCCCTTGT 1077

Human: TATCCATTTGTCACAAAGGCTTCTGAAATAATTGTATAAAAGCAACTCTACCATACAAACAGTGGTCAATTCTTAACTTCTGAGGAAGGGATTCAGGCCACCA---CACACCGCTCAATTCCACTGTA 1173  
 Guinea Pig: TATCCATTTGTCACAAAGGCTTCTGAAATAATTGTATAAAAGCAACTCTACCATACAAACAGTGGTCAATTCTTAACTTCTGAGGAAGGGATTCAGGCCACCA---CACACCGCTCAATTCCACTGTA 1173  
 Mouse: TACCTTGTGTCACAGCGTTCAGAGGCTTCTGGAGATACTTGTGIGIGCAAGAACCGACCGCTGTAA---CAGACCCAGTCAGTATCTCTGTA 1176  
 Rat: TACCTTGTGCCACAGACGTTCCAGAAGGCTTCTGGAGATACTTGTGIGIGCAAGAACCGACCGACTTCA---CAGACCCAGTCAGTATCTCTGTA 1176

Figure 8  
Amino Acid sequence Comparison of Human (SEQ ID NO:2), Guinea Pig (SEQ ID NO:10),  
Mouse (SEQ ID NO:8) and Rat H4 (SEQ ID NO:9)

Docket No.: PRD-0033  
App No.: not yet assigned Filed: herewith  
Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE  
Inventors: Timothy Lovenberg and Changlu Liu  
Attorney: Felicity E. Groth Phone: (215) 568-3100  
Sheet 13 of 13

Human:	SVYNIVLISYDRYLSVSNASVSYRTQHTGVLKIVTLMVAVVLAFLVNGPMILVSESMWKDEG-S-ECEPGEFSEWYIILAITSFLEFVIPVILVAYFNMVY	198
Guinea Pig:	SVYNIVLISYDRYQSVSNASVWYRAQHSGTWKIAQTMVAVNIFSFMTNGPMILISDWONST-T-ECEPGEFLKKWYFALPTSLEFLIPLVAYFSAHY	197
Mouse:	SVYNIVLISYDRYQSVSNASVYRAQHTGIMKIVAQMVAVNIALFLVNGPMILASDWKNSTNTKDCEPGFVTEWYIITIMLLEFLIPVISVAYFNVQY	200
Rat:	<u>SVYNIVLISYDRYQSVSNASVYRAQHTGILKIVQMVAVNIALFLVNGPMILASDWKNSTNTKDCEPGFVTEWYIITIMLLEFLIPVISVAYFNVQY</u>	200
Consensus:	<u>SVYNIVLISYDRY SVSNASV YR:QH:G. KI. MAWN::F:NGPMIL:S:SW:.. : CEPGF:..WY::T:LEF::P::WAYF::IY</u>	TM4
Human:	WSLWKRDHLSRCQSHPGI-TAVSSNTICGHSFRGRISRRSLSASTEPFHSEQRKRSSLMFSSRTKMNNSNTIASKMGSFSQSDSVALHQREHVELR	297
Guinea Pig:	WSLWKREKLSRCLSHPVLPSPDSRSLT PARKETTASLGSDSKRSSLFSIRAYKNSNVIASKMGLFLSHSDSLALQREHIELFR	297
Mouse:	WSLWKRRALSRCPSHAGF-STTSSASASGLHLHRAGVACRTSNPGIKAESAAASRHSESPRKSSILVSLRTHMNNSITAFKVGSFWRSESAIRREYAEILLR	299
Rat:	WSLWKRGSLSRCPSHAGF-IATSSRGTGHSRRTGLACRTSLPGLKEPAAASLHSESPRGKSSLVSLRTHMSGSIITAFKVGSFCRSESPVILHQIEHVELR	299
Consensus:	<u>WSLWKR:LSRC SH. : :. SS. GH. R .:R ::::E..AS: S: R. KSSL: S R: . . . . A.K:G : :S:S: L:Q E:EL:R</u>	TM5
Human:	ARRLAKSLAILIGVFACWAPYSLFTTIVLSFYSSATGPKSVWYRIAFLQWFNSFVNPLLYPLCHKRFQOKAFLKIFCIIKKQPLPSQHRSRVSS	390
Guinea Pig:	ARRLAKSLAILAFACTCWAQPSLTTIVIYSSFFPERNLTKSTWYHTAFFLQWFNSFVNPLLYPLCHKRFQOKAFLKILPVRROSTPP-HNRSIST	389
Mouse:	GRKLARSLAILISAFACIWCAPYCLFTTIVLSTYPRTERPKSVWYIAFLQWFNSFVNPLLYPLCHRRFQKAFWKLICVTKQPAQALSQ-NQSVSS	391
Rat:	GRKLARSLAVLISAFACIWCAPYCLFTTIVLSTYRRGERPKSIWYIAFLQWFNSLNPFLYPLCHRRRFQKAFWKLICVTKQPAQSS-TQSVSS	391
Consensus:	<u>R:LA:SLA:LL:FA:CWAPY:L T: S : :. . KS.WY:AEFLQWENS:NP:LYPICH:RFQKAF.KI: ::Q: : :RS:S:</u>	TM7